REMARKS

INTRODUCTORY COMMENTS:

Claims 1, 2, and 6 to 8 are currently pending. In the current Office Action, the Examiner has rejected the claims on the following grounds:

1. Under 35 U.S.C. §112, first paragraph, as containing subject matter not described in the specification in such a way as to reasonably convey that the inventor had possession of the claimed subject matter at the time of filing;

2. Under 35 U.S.C. §112, first paragraph, as lacking enabling disclosure in the specification;

3. Under 35 U.S.C. §112, second paragraph, as indefinite; and

3. Under 35 U.S.C. §103(a) as obvious over PCT Publication WO 96/34626, in view of PCT Publication WO 92/16556 and U.S. Patent No. 5,795,862 to Frank et al.

Additionally, the Examiner has requested that a new oath or declaration be filed as the existing declaration does not include the applicants' complete residence addresses.

With the above amendments, claims 3 and 9-14 have been canceled as drawn to non-elected inventions. Thus, claims 1, 2, and 6-8 are now pending. The rejections are addressed in part by the above amendments and in part by the arguments that follow.

THE AMENDMENTS:

Claims 3 and 9-14 have been canceled as drawn to non-elected inventions. Cancellation of these claims is without prejudice, without intent to acquiesce in any rejection of record, and without intent to abandon any previously claimed subject matter.

Claim 1 has been amended to specify that the pharmaceutical composition is capable of selectively enhancing TH_1 response and to specify that the composition comprises an allergen or an allergen extract. Support for this amendment is found on page 1, lines 8 to 31, page 2, lines 9-14, and in preparation 1 on page 4 of the specification. Accordingly, no new matter has been entered.

THE REQUEST FOR A NEW DECLARATION:

The Examiner has request a new oath or declaration stating that the Declaration filed with the application is defective in that the inventors' full addresses are not set out. Applicants invite the Examiner to review the Declaration again where she will see that inventor Ulrich's complete residence address is in fact given (883 Hamilton Heights Road, Corvallis, Montana 59828, U.S.A.) as is inventor Wheeler's complete residence address (70 Littlehaven Lane, Hosham, West Sussex RH12 4SB, GB). Withdrawal of the objection to the Declaration is accordingly requested.

THE REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH, REGARDING THE WRITTEN DESCRIPTION:

The Examiner has rejected all claims under 35 U.S.C. §112, first paragraph, as failing to satisfy the written description requirement. The Examiner specifically states that while the pending claims recite a pharmaceutical composition that is optionally modified in some way, there is insufficient disclosure in the specification of such a modified allergen. Applicants disagree.

The premises upon which the Examiner bases the rejection are as follows:

1. An adequate written description of a "modified allergen" requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention, citing *Fiers v. Revel* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993).

2. The term "optionally modified allergen" without more is not an adequate written description of a genus because it does not distinguish the claimed genus from others, except for by the property of the allergen having been modified. As a consequence, one of skill in the art cannot visualize or recognize the identity of the members of the genus.

3. A definition by the property of having been modified does not suffice to define the genus because it is only a definition of a useful result rather than a definition of what achieves that result. The Examiner supports this premise by citing *In re Wilder* 222 U.S.P.Q. 369, 372-73 (Fed. Cir. 1984).

Applicants disagree and submit that the Examiner is misinterpreting the written description requirements. As stated in The Revised Interim Guidelines for the Examination of Patent Applications (1999) Federal Register 64(244):71427-71440, in the first paragraph of section I.A, "[t]here is a strong presumption that an adequate written description of the claimed invention is present when the application is filed." The Guidelines further state that "[t]he absence of definitions or details for well-established terms or procedures should not be the basis of a rejection under 35 U.S.C. §112, first paragraph, for lack of adequate written description."

In the present instance, the meanings of the terms "modified allergen" or "optionally modified allergen" are well known and established in the field and describe any form of cross linking or polymerization. This modification may result in intermolecular or intramolecular linkages, and may produce thereby homopolymers or heteropolymers. The fact that the term "modified" as applied to the term allergen is readily understood by those skilled in the art should be clear from the following references, all of which are over 20 years old, supplied by the applicant:

Marsh D. G. (1971), "Preparation and Properties of Allergoids Derived from Native pollen Allergens by Mild Formalin Treatment," *Int. Achs. Appl. Immun.* 41:199-215;

March et al. (1970), "Studies on Allergoids Prepared from Naturally Occurring Allergens," *Immunology* 18:705-722;

Patterson et al. (1973), "Polymerized ragweed antigen E (I) Preparation and Immuological Studies," *J. Immun.* 110:1402-1412;

Patterson et al. (1973), "Polymerised ragweed antigen E (II) In Vivo Elimination Studies and Reactivity with IgE antibody Systems," *J. Immun.* 110:1413-1418;

Patterson et al. (1974), "Polymerised ragweed antigen E (III) Differences in Immune Response to Three Molecular Weight Ranges of Monomer and Polymer," *J. Immun.* 112:1855-1860;

Sri-Ram et al. (1962), "Chemical Modification of Proteins and their Significance in Enzymology, Immunochemistry and Related Subjects," *Adv. Enxymol.* 24:105-160;

Wheeler et al. (1976), "Chemical Modification of Crude Timothy Grass Extract (II) Class and Specificity of Antibodies Induced by Chemically Modified Timothy Grass Pollen Extract," *Int. Ach. Allergy Appl. Immunol.* 50:709-728; and

Moran et al. (1977), "Chemical Modification of Crude Timothy Grass Extract (III) The Effect of Glutaraldehyde Induced Aggregation on Antigenic and Immunogenic Properties," *Int. Ach. Allergy Appl. Immunol.* 55:315-321.

In response to the Examiner's first premise, i.e., that an adequate written description of a "modified allergen" would require an explicit definition, applicants submit that given the level of knowledge in the immunological field regarding modified allergens, an explicit definition is not required. As stated in the Interim Guidelines, "[w]hat is conventional or well known to one skilled in the art need not be disclosed in detail. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly describe in the specification, then the adequate description requirement is met."

Furthermore, In *Fiers v. Revel,* the case cited by the Examiner, the claims were drawn to a specific DNA sequence that had not been specifically disclosed in the specification. The subject matter of the present invention does not involve one specific modified allergen. Rather,

the present invention is drawn to a composition that may comprise any allergen, modified or not, tyrosine, and 3-DMPL.

In response to the Examiner's second premise, i.e., that one of skill in the art cannot visualize or recognize the identity of the members of the genus as the term "optionally modified allergen" does not distinguish the claimed genus from others, applicants once again submit that given the conventional and well-known meaning of what constitutes a modified allergen, as evidenced by the above-indicated references, one of skill in the art would have no difficulty understanding the scope of the claimed genus of modified allergens.

The Examiner's third premise also fails to take into consideration the well-known understanding of allergen modification. The Examiner has cited *In re Wilder* for its language regarding a specification that presents little more than an outline of the goals an applicant hopes the invention will achieve and the problems the invention will ameliorate. However, in *In re Wilder,* the patentee seeking broader claims on reissue attempted to use the statements made in the "Objects of the Invention" section of the specification to support the new claims. While the specification disclosed only specific embodiments of the claimed invention (utilization of synchronous scanning equipment), the new claims did not require such equipment.

The circumstances in the present case are in no way similar to those of *In re Wilder.* **In claiming a composition comprising an optionally "modified allergen," applicants are not simply outlining a goal, they are reciting a well-known and commonly understood genus. The goal of the invention is not to modify an allergen; rather, it is to provide a composition comprising an allergen that can be optionally modified using well-known techniques, tyrosine, and 3-DMPL.**

Given the commonly understood meaning of an "optionally modified allergen," applicants submit that one of ordinary skill in the art would have no difficulty realizing that applicants were in possession of the claimed subject matter when the application was filed. The rejection is thus in error and its reconsideration and withdrawal is respectfully requested.

THE REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH, REGARDING ENABLEMENT:

The Examiner has rejected claims 1, 2, and 6-8 on the ground that the specification does not provide enablement for a pharmaceutical composition comprising an optionally modified

allergen. Applicants disagree. As discussed above, the term "modified allergen" is a term well known in the field and encompasses all manner of crosslinked and polymerized allergens. The term is perfectly understood by one of skill in the art and, given that understanding, one of ordinary skill in the art would clearly be enabled by the disclosure provided by the specification to formulate the claimed composition. Reconsideration and withdrawal of the rejection is accordingly in order and is respectfully requested.

THE REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH.

The Examiner has rejected all claims under 35 U.S.C. §112, second paragraph, as indefinite. Claims 2 and 6-8 have been rejected for their use of the word "the" to reference previously recited claim elements, and claim 1 has been rejected for its use of the term "optionally modified." Applicants disagree with all aspects of the rejection.

The rejection regarding the use of "the" is in error as such usage is customary and accepted in PTO practice. If the Examiner will refer to section 2173.05 (e), she will see that expressions such as "the tyrosine" and "the allergen" do not constitute indefinite claim language. Claim 1 clearly recites "tyrosine" and an "allergen" and there would be no confusion regarding exactly which tyrosine or allergen was intended in the claims dependent therefrom. As stated in *Ex parte Porter*, 25 USPQ2d, 1144, 1145 (Bd. Pat. App. & Inter. 1992), if the scope of a claim would be reasonably ascertainable by those skilled in the art, then the claim is not indefinite. In the present case, "the tyrosine" and "the allergen" clearly refer to the allergen and the tyrosine recited in claim 1. Reconsideration and withdrawal of the rejection with respect to claims 2 and 6-8 are in order and are respectfully requested.

With regard to the rejection of claim 1 for its usage of the term "optionally modified," applicants have amply demonstrated above that the concept of a modified allergen is well known and understood in the art. The scope of claim 1 is clearly understandable to one of ordinary skill in the art and the claim is in no way indefinite. Reconsideration and withdrawal of the rejection of claim 1 are accordingly requested.

THE REJECTION UNDER 35 U.S.C. §103(a):

The Examiner has rejected all claims as obvious over the teaching of WO 96/34626 (Wheeler et al) in view of WO 92/16556 (Van Wijnendale et al.) and U.S. Patent No. 5,795,862 to Frank et al. Wheeler et al. has been cited as disclosing a pharmaceutical composition comprising tyrosine and an optionally modified allergen. Van Wijnendale et al. is cited as disclosing a pharmaceutical composition comprising a modified or unmodified peptide antigen and 3D-MPL as an adjuvant. Frank et al. has been cited as disclosing a therapeutic composition for use in desensitization therapy, the composition containing at least one isolated flea saliva protein allergen, an adjuvant, and a carrier. The Examiner concludes that the combination of these teachings renders the pending claims obvious. Applicants disagree.

As amended, independent claim 1 recites a pharmaceutical composition capable of selectively enhancing TH_1 response comprising tyrosine, an optionally modified allergen, and 3-DMPL. The invention is based on the important observation that 3-DMPL can enhance the T cell TH_1 response to an allergen over the TH_2 response. In an allergic subject, the preferential TH_1 response can bring about important clinical benefits; see page 1, lines 8 to 31, of the specification.

To establish *prima facie* obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify a reference or to combine reference teachings. Second, there must be a reasonable expectation of success, and third, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). In the present case, these three requirements have not been met.

Wheeler et al. discloses a pharmaceutical composition comprising tyrosine and a polymerized allergen. As acknowledged by the Examiner, the reference does not disclose or discuss the inclusion of 3-DMPL or any other adjuvant in the composition. There is nothing in Wheeler et al. that suggest that 3-DMPL should or could be included in the formulation.

Van Wijnendale et al. discloses an assertedly novel form of gb160 and a vaccine formulation containing the gp160 and 3-DMPL. On page 8, lines 26 to 29, Van Wijnendale et al. teaches that, in the context of the prophylactic and therapeutic treatment of HIV infections, 3-DMPL is able to stimulate both arms (i.e., the neutralizing antibody and the effector cell-mediated immunity) of the immune system. **The application, however, does not teach or suggest that 3-DMPL can be used more widely as a general adjuvant in vaccine formulations**. Furthermore, Van Wijnendale et al. does not teach or suggest that 3-DMPL is suitable for use in allergen formulations and certainly not in formulations comprising tyrosine and optionally polymerized allergens. Moreover, there is nothing in Van Wijnendale et al. that would lead one of ordinary skill in the art to believe that 3-DMPL is able to promote the preferential TH_1 activity desired in allergen formulations, but not necessarily desired in vaccine formulations intended to treat and/or offer protection against infectious diseases such as HIV.

Thus, there is nothing in either Wheeler et al. or Van Wijnendale et al. that would motivate one of ordinary skill in the art to include 3-DMPL in the allergen formulation disclosed by Wheeler et al. The Examiner has cited Frank et al. for its disclosure of a composition containing at least one isolated allergen, an adjuvant, and a carrier and presumably relies upon this disclosure for a motivation to combine the adjuvant 3-DMPL with the composition of Wheeler et al. While Frank et al. does disclose the possibility of the inclusion of an adjuvant, **the reference contains no teaching or suggestion regarding the inclusion of 3-DMPL**. It is only via the benefit of impermissible hindsight that the Examiner is able to select Van Wijnendale et al., which discloses the use of 3-DMPL in a different composition for a different purpose, and suggest that its teaching be combined with that of Wheeler et al. and Frank et al. As there is no motivation to combine the teaching of 3-DMPL in Van Wijnendale et al. with the teaching of Wheeler et al. and Frank et al. the first criterion has not been met.

The second criterion for *prima facie* obviousness has also not been met. There would be no reasonable expectation of obtaining a composition capable of selective TH_1 response enhancement by combining the teachings of the three references. The knowledge that 3-DMPL selectively enhances TH_1 response was completely unknown prior to discovery by the applicants. For this same reason, the third criterion has also not been satisfied. The combination of

references clearly fails to teach or suggest that a 3-DMPL-containing composition would selectively enhance TH_1 response.

For the above reasons, the cited combination of references fails to establish *prima facie* obviousness. The rejection of claim 1 is in error, as is the rejection of all claims dependent therefrom, i.e., claims 2 and 6-8. Reconsideration and withdrawal of the rejection are in order and are hereby requested.

CONCLUSION

For the foregoing reasons, applicants submit that the claims are patentable over the art and satisfy all requirements of 35 U.S.C. §112. A Notice of Allowance is requested, and a prompt mailing thereof would be much appreciated.

If the Examiner has any questions concerning this communication, please contact the undersigned at (650) 330-0900.

Respectfully submitted,

Date: 10/5/01

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APPENDIX A

REDACTED SPECIFICATION AND CLAIMS INDICATING AMENDMENTS MADE

IN THE CLAIMS

Please amend claim 1 as indicated below. Text to be deleted is indicated as ~~deleted text~~, while added subject matter is underlined.

1. (Amended) A pharmaceutical composition capable of selectively enhancing TH_1 response comprising tyrosine, an optionally modified allergen or allergen extract, and 3-DMPL.